REMARKS

Applicants have amended claims 1-5 and 11. Applicants have canceled claim 8.

In Claim 1, the recitation "which binds to EGFR" has been added support for which may be found in paragraphs [0008], [0039], and [0049], for example. The recitation "one or more complementarity determining regions selected from the group consisting of" has been deleted. Applicants have also added the terms "and" and "or" to claim 1. In Claims 2-5, Applicants have corrected the spelling of the word "fragment." In Claim 11, Applicants have changed "an" to "a." Also in Claim 11, the recitation "Fc, bivalent fragments (Fav) 2, and single domain antibody" has been added, support for which is found in paragraphs [0036]-[0038] of the specification, for example.

Accordingly, no new matter has been added by these amendments. Entry of these amendments is respectfully requested.

PRIORITY

The Examiner alleged that Sequences 2, 4, 6, 8, 10, 12, 14 and 16 were not disclosed in the provisional Applications. Applicants respectfully disagree in that SEQ ID NOS. 2, 4, 6, 8, 10, 12, 14, 16 correspond to SEQ ID NOS. 1, 3, 5, 7, 9, 11, 13, 15 respectively of provisional applications 60/554,555 and 60/624,264.

Accordingly, Applicants respectfully request reconsideration and priority to provisional Applications 60/554,555 and 60/624,264.

CLAIM REJECTIONS UNDER 35 USC § 112

Claims 1-5 and 8-13 have been rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the

written description requirement. Applicants respectfully disagree.

Paragraph [0008] of the Application states that:

> [T]he antibodies of the present invention, or fragments thereof, comprise SEQ ID NO:2, SEQ ID NO:4, and SEQ ID NO:6. Alternatively, but also preferably, the antibodies of the present invention, or fragments thereof, comprise SEQ ID NO:10, SEQ ID NO:12, and SEQ ID NO:14…. Such antibodies or fragments thereof of the present invention have various properties, including the ability to neutralize EGFR and prevent binding of a ligand of EGFR to its receptor.

(emphasis added)

Applicants have amended Claim 1 to recite an isolated antibody or antibody fragment, which binds to EGFR that comprises SEQ ID NO:2 at CDRH1; SEQ ID NO:4 at CDRH2; and SEQ ID NO:6 at CDRH3; or SEQ ID NO:10 at CDRL1; SEQ ID NO:12 at CDRL2; and SEQ ID NO:14 at CDRL3.

In addition, paragraph [0048] makes it clear that the antibody, or fragments thereof, can have a heavy chain variable region of SEQ ID NO:8 and/or a light chain variable region of SEQ ID NO:16 and further defines SEQ ID NO:8 as including three CDRs (SEQ ID NOS:2, 4, 6) and SEQ ID NO:16 as including three CDRs (SEQ ID NOS:10, 12, 14). That same paragraph also refers to IMC-11F8 as a "preferred antibody of the present invention."

Thus, Applicants have sufficiently described antibodies comprising either 3 specific light chain CDRs or 3 specific heavy chain CDRs in the specification as to reasonably convey to one skilled in the art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

As demonstrated, the application clearly sets forth an antibody with the three CDRs of the heavy chain or the three CDRs of the light chain. Claims 2-5 and 8-13 are dependent from

Claim 1 and thus, also clearly set forth the invention as described in the specification.

The Examiner has also rejected claim 12 because the conjugate of the antibody is missing one key element, the conjugation partner and there is no description of the possible conjugation partner so as to adequately describe the claim. Applicants respectfully disagree.

Paragraph [0041] of the specification states:

> As used herein, "antibodies" and "antibody fragments" includes modifications that retain specificity for the EGF receptor. Such modifications include, but are not limited to, conjugation to an effector molecule such as a chemotherapeutic agent (e.g., cisplatin, taxol, doxorubicin) or cytotoxin (e.g., a protein, or a non-protein organic chemotherapeutic agent). The antibodies can be modified by conjugation to detectable reporter moieties. Also included are antibodies with alterations that affect non-binding characteristics such as half-life (e.g., pegylation).

Also, in paragraph [0104] it is stated that "in a preferred embodiment, biotin is conjugated to an anti-EGFR antibody" and that "alternatively, biotin or another such moiety is linked to an anti-EGFR antibody of the invention and used as a reporter, for example in a diagnostic system where a detectable signal-producing agent is conjugated to avidin or streptavidin."

In addition, paragraph [0042] states that conjugation to antibodies may be performed by methods that are known in the art and include direct linkage, linkage via covalently attached linkers, and specific binding pair members (e.g., avidin-biotin). Other methods have been described by Greenfield *et al.*, Cancer Research 50, 6600-6607 (1990) for the conjugation of doxorubicin, by Arnon *et al.*, Adv. Exp. Med. Biol. 303, 79-90 (1991) and by Kiseleva *et al.*, Mol. Biol. (USSR)25, 508-514 (1991) for the conjugation of platinum compounds. Thus, Applicants have sufficiently described possible conjugation partners in the specification. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

Claims 1-13 have been rejected under 35 USC § 112, first paragraph. The Examiner has determined that the specification, while being enabling only for an isolated antibody comprising all six CDRs (3 CDRs of a heavy chain amino acid sequence and 3 CDRs of a light chain amino acid sequence) and which binds to EGFR, does not reasonably provide enablement for antibodies that have any of the above mentioned sequences missing or fragments of the antibodies and without the knowledge whether it binds to a specific antigen such as EGFR. Applicants respectfully disagree.

Applicants have enabled any person skilled in the art to make and use the invention. In fact, paragraph [0045] details the methods by which binding characteristics of the antibodies of the present invention may been improved, improving affinity and specificity, and ways to mutate the CDRs to yield the antibodies of the present invention. Paragraph [0045] states:

> Antibodies of the present invention further include those for which binding characteristics have been improved by direct mutation, methods of affinity maturation, phage display, or chain shuffling. Affinity and specificity can be modified or improved by mutating CDRs and screening for antigen binding sites having the desired characteristics (*see, e.g.*, Yang et al., J. Mol. Biol., 254: 392-403 (1995)). CDRs are mutated in a variety of ways. One way is to randomize individual residues or combinations of residues so that in a population of, otherwise identical antigen binding sites, all twenty amino acids are found at particular positions. Alternatively, mutations are induced over a range of CDR residues by error prone PCR methods (see, *e.g.*, Hawkins *et al.*, J. Mol. Biol., 226: 889- 896 (1992)). For example, phage display vectors containing heavy and light chain variable region genes can be propagated in mutator strains of E. coli (*see, e.g.*, Low *et al.*, J. Mol. Biol., 250: 359-368 (1996)). These methods of mutagenesis are illustrative of the many methods known to one of skill in the art.

In addition, paragraph [0055] details production of antibody fragments by "cleaving a whole antibody or by expressing DNA that encodes the fragment." It is also demonstrated that preparing fragments of antibodies are well known in the art. *See* Lamogi *et al.*, *J. Immunol. Methods*, 56:235-243 (1983) and by Parham, *J. Immunol.* 131:2895-2902 (1983), both of which are included in the specification.

Thus, it appears that one skilled in the art could use the methods as described in paragraphs [0045] and [0055] to arrive at the present invention. Clearly, one skilled in the art would understand chain shuffling and creation of antibody fragments and know how to use those methods in order to derive antibodies or fragments thereof from the specifically recited antibodies.

Indeed, employing any of the above methods to arrive at the claimed invention is not undue experimentation despite what may be considered a large quantity of experiments. In fact:

> [T]he test [for undue experimentation] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention.

Johns Hopkins University v. Cellpro, Inc., 152 F.3d 1342 (Fed. Cir. 1998).

In this particular instance, the experiments are merely routine and one of ordinary skill in the art would need very little guidance or working examples in order to perform the above described methods to create antibodies or fragments of the present invention. As such, this experimentation cannot be considered unduly burdensome.

Also, Claim 1 contains the recitation "antibody or antibody fragment which binds to EGFR." Examples 5-7 in the specification describe methods of determining whether a particular antibody binds to EGFR. These methods are routine and well-known in the art. Claims 2-13 are dependent from Claim 1 and thus, are also properly enabled. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

CLAIM REJECTION 35 USC § 102

Claims 1 and 8-13 have been rejected under 35 U.S.C. § 102(b) over Jakobovits *et al.* (US 6,235,883), Siegel *et al.* (WO2004/005890), and Deo *et al.* (WO03/064606), all of which recite one or two sequences which are recited in Claim 1. Claim 1 has been amended to specify that the antibody contain at least 3 CDR sequences. None of the references relied upon by the Examiner recite all 3 of these sequences. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

As it is believed that all of the rejections set forth in the Official Action have been fully met, favorable reconsideration and allowance are earnestly solicited.

If, however, for any reason the Examiner does not believe that such action can be taken at this time, it is respectfully requested that she telephone Applicants' attorney at (908) 654-5000 in order to overcome any additional objections which she might have.

If there are any additional charges in connection with this requested amendment, the Examiner is authorized to charge Deposit Account No. 12-1095 therefor.

Dated: September 25, 2008 Respectfully submitted,

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